## REMARKS

Reconsideration of the subject application is respectfully requested. Claims 1-14 are pending in his application.

Turning to the amendments noted above, the specification has been amended to insert a title that was inadvertently omitted when the application was translated into English. The amendments to claims 12-14 place those claims in more typical U.S. format. No new matter has been added by the foregoing amendments.

Turning to the rejections, claims 12-14 stand rejected under Section 112 and Section 101. Claims 12-14 have been amended to place the claims in more typical U.S. claim format and have not been amended in any substantive fashion. Applicant submits that the amended claims 12-14 are in compliance with Section 112 and Section 101.

Claims 1-14 stand rejected under Section 103(a) as allegedly being unpatentable over Ibrahim (U.S. Patent No. 5,716,988) in combination with Schilpalius (U.S. Patent No. 5,897,871) or Blackshear (U.S. Patent No. 4,439,181). For the following reasons, Applicant respectfully submits that the cited prior art fails to disclose or suggest the claimed invention.

With respect to the primary reference, Ibrahim does not describe nor suggest any method allowing the concentration of oxaliplatinum to be at least 7 mg/ml, especially by adding any of the hydroxylated components as specifically identified in claim 1. In this regard, Ibrahim corresponds to the International patent application WO96-04904 cited in the International Search Report. In the International Search Report, this reference was categorized as an "A" reference – i.e., as a document defining "the general state of the art **which is not considered to be of particular relevance**" to the claimed invention.

Fairly stated, Ibrahim merely describes a pharmaceutical preparation of oxaliplatinum, where the oxaliplatium is dissolved in water at a concentration in the range from 1 to 5 mg/ml (see Col. 2, lines 9 to 13), preferably at a concentration of 2 mg/ml (see Col. 2, lines 20 to 22). According to Example 1, the preparation is obtained by adding the specified amount of oxaliplatinum in warm water. It is mentioned in Col. 2, lines 17 to 18, that this preparation is free of any other components. Solubility of oxaliplatinum in pure water is known as being 7.9 mg/ml. See the attached The Merck Index Online, Oxaliplatin. Accordingly, in an aqueous preparation of oxaliplatinum obtained according to Ibrahim, the concentration of oxaliplatinum cannot be higher than 7.9 mg/ml. Furthermore, due to the risk of precipitation under proper storage and handling conditions for such a pharmaceutically stable aqueous preparation of oxaliplatinum as obtained according to Ibrahim, the concentration of oxaliplatinum must be less than or equal to 5 mg/ml. Thus, Ibrahim does not describe or suggest any method allowing the concentration of oxaliplatinum of higher than 7 mg/ml, especially by adding any of the hydroxylated components as identified in claim 1 of the subject application.

The secondary references do not overcome the deficiencies of the primary reference. For example, Schlipalius does not describe or suggest any method leading to a pharmaceutically stable preparation of oxaliplatinum as claimed in claim 1 of the subject application. This reference merely describes a method for obtaining a beta-carotene composition under an emulsified form. See Col. 5, lines 41 to 49; and Col. 5, line 53, to Col. 6, line 11. To that end, this particular composition comprises a dispersible component and an emulsifier component. See Col. 2, lines 57 to 63. The dispersible component may be selected from an unlimited series of undefined agents. See Col. 2, line 66, to Col. 3, line 5. Among those dispersible components, glycerol is preferred. See Col. 3, line 69. According to the details of the emulsified beta-

carotene composition given in the Example and, in particular, the respective amount of water (Col. 5, lines 53 to 64), such a composition cannot be considered as being an aqueous composition. As a result, there is no motivation for a person skilled in the art, looking for an aqueous liquid formulation of the organo-metallic complex oxaliplatinum and taking into account the respective chemical, physical and pharmacological properties, to consider any document dealing with the formulation of beta-carotene. Furthermore, this person skilled in the art would find in the teaching of Schlipalius only a method for the preparation of non-aqueous emulsified composition of an active compound, i.e. beta-carotene. For all of these reasons, this secondary reference would not and could not be combined with the primary reference to render the claimed invention obvious.

Like Schlipalius, Blackshear does not describe or suggest any method leading to a pharmaceutically stable preparation of oxaliplatinum as claimed in claim 1 of the subject application. This document merely describes a method for maintaining fluidity of protein solutions, for example, insulin solution, for parenteral administration (see Col. 2, lines 61 to 66) in order to prevent precipitation of said proteins during long-term storage (see Col. 3, lines 3 to 5). To that end, it is proposed to admix a polyol solution, for instance glycerol, with the solution of the protein, so that the final concentration of polyol in the solution is allowed to reach 90% by volume. Clearly, under such a condition, the obtained solution cannot be considered as being an aqueous solution. And, like Schlipalius, there is no motivation for a person skilled in the art, looking for an aqueous liquid formulation of the organo-metallic complex oxaliplatinum and taking into account the respective chemical, physical and pharmacological properties, to consider any document dealing with formulation of a protein. Furthermore, this person skilled in the art

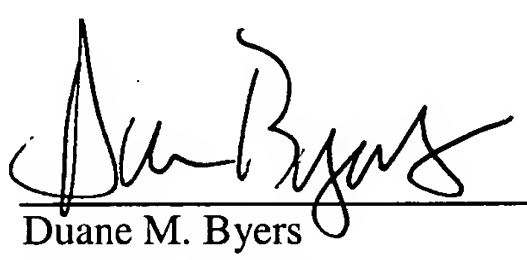
would find in the teaching of Blackshear only a method for the preparation of non-aqueous composition of an active compound, i.e. insulin.

In view of the foregoing comments and a proper reading of the references, Applicant submits that the primary reference and the two secondary references do not disclose or suggest the claimed invention. Accordingly, Applicant requests the withdrawal of the Section 103(a) rejection.

Applicant respectfully requests that a timely Notice of Allowance be issued in this case.

Respectfully submitted,

**NIXON & VANDERHYE P.C.**

By: 

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06981 **Monograph Name:** Oxaliplatin
CAS REGISTRY NUMBER: 61825-94-3
MOLECULAR FORMULA: C8H14N2O4Pt MOLECULAR WEIGHT: 397.29
MOLECULAR COMPOSITION: C 24.19%, H 3.55%, N 7.05%, O 16.11%, Pt 49.10%
C.A. CHEMICAL NAME(s): (SP-4-2)-((1R,2R)-1,2-Cyclohexanediamine-kappaN,kappaN')(ethanedioato(2-)-kappaO1,kappaO2)platinum
SYNONYMS:
((1R,2R)-1,2-cyclohexanediamine-N,N')(oxalato (2-)-O,O')platinum ; oxalato (1R,2R-cyclohexanediamine)platinum(II) ; Pt(oxalato)(trans-l-dach) ; oxalato (trans-1-1,2-diaminocyclohexane)platinum (II) ; oxalatoplatin ; oxalatoplatinum ; 1-OHP
DRUG CODES: RP-54780; NSC-266046
BRAND NAME (and COMPANY):
Eloxatin (Sanofi-Synthelabo)
LITERATURE REFERENCES:
Third generation platinum complex. Prepn and antitumor activity: Y. Kidani et al., J. Med. Chem. 21, 1315 (1978); Y. Kidani et al., Gann 71, 637 (1980). Crystal structure: M. A. Bruck et al., Inorg. Chim. Acta 92, 279 (1984). FAB and LAMMA MS analysis: J. Claereboudt et al., J. Pharmaceut. Biomed. Anal. 7, 1599 (1989). Pharmacokinetics: R. Kizu et al., Cancer Chemother. Pharmacol. 31, 475 (1993). Clinical evaluation in colorectal cancer: F. Levi et al., Eur. J. Cancer 29A, 1280 (1993). Brief review of antitumor and clinical activity: G. Mathe et al., Biomed. Pharmacother. 43, 237-250 (1989).
PHYSICAL DATA:
Colorless, thin triangular plates with truncated vertices. Sol in water 7.9 mg/ml.
THERAPEUTIC CATEGORY: Antineoplastic.
REFERENCE KEYS PRESENT: Activity; Analysis; Clinical evaluation; Prepn; Review; Structure
DATA KEYS PRESENT: Molecular Weight; Therap. Cat.